REMARKS

New claim 30 is supported by claim 6.

The undersigned thanks the Examiner for the courtesies extended during the telephone interview of May 16, 2007. During the interview, the undersigned explained that the Examiner's position that Aksay teaches the claimed method directed to molecular combining *of a biomolecule* wherein the molecular combining comprises attachment of the biomolecule to a surface and alignment of the biomolecule is incorrect. The undersigned explained that Aksay teaches a method of making "[a] process directed to preparing surfactant-polycrystalline *inorganic nanostructured materials* having designed microscopic patterns" (see abstract, lines 1-3, of Aksay; emphasis added) that mimic natural structures found in nature, but it does not teach the claimed method directed analyzing a biomolecule.

The Examiner stated that he has broadly interpreted "biomolecule," and stated a definition of "biomolecule" from the Internet to mean "any organic molecule that is an essential part of a living organism." *See* "Definitions of Biomolecule on the Web" at http://www.google.com/search?hl=en&defl=en&q=define:Biomolecule&sa=X&oi=glossary_definition&ct=title. The undersigned explained that even by this broad definition of "biomolecule" from the web, the "surfactant-polycrystalline *inorganic nanostructured materials* having designed microscopic patterns" (see abstract, lines 1-3, of Aksay; emphasis added) are outside the scope of the claimed invention because "inorganic nanostructured materials" are not "any organic molecule that is an essential part of a living organism."

The undersigned also explained that all of the portions of Aksay cited by the Examiner only relate to making *inorganic* nanostructures that *mimic* products of nature, but do not relate to molecular combining *of a biomolecule* wherein the *molecular combining* comprises attachment of the biomolecule to a surface and alignment of the biomolecule. In fact, nowhere does Aksay disclose molecular combining of any material whatsoever. The undersigned explained that the first inventor of Aksay is Professor Ilhan A. Aksay, Professor of Chemical Engineering and Ceramics Materials Laboratory, Princeton University. See attached Exhibit 1. Professor Aksay's research is

not in biomolecules, but instead in biometrics and bioinspired processing of *ceramic "[c]omposite materials* with structure patterned after biological systems" which "has led to the development of improved *ceramic* fabrication processes, mainly through the use of colloidal dispersion and consolidation methods." *See* attached Exhibit 2, page 1, paragraph 1, line 14, and paragraph 2, lines 1-2; emphasis added. In short, Aksay relates to *inorganic* nanostructures that *mimic* products of nature, but do not relate to molecular combining *of a biomolecule*. The Examiner said that the undersigned should include these arguments on the record, and he would carefully consider them in consultation with other Examiners in the USPTO. The undersigned thanked the Examiner for his willingness to re-consider this case in light of the arguments put forth by the undersigned.

Claims 1-2, 4-7, 12-13, 24-26 and 28-29 were rejected as being obvious over Kley in view of Aksay. This rejection is respectfully traversed.

On page 2, lines 9-13, of the Action, under the "Response to Amendment and Arguments" filed December 12, 2006, the Examiner states:

> Aksay teaches a concept of a biomolecule (page 5, column 1, [0055])) which [is] also well known in the art (page 1, column 1, [0004]) wherein the molecular combining attachment of the biomolecule to a surface (abstract, first 10 lines) and alignment of the biomolecule (the alignment of nanostructures which disclosed by Aksay can be biomolecule) (page 2, column 2, [0023]; page 3, column 2, [0036]).

Let us review all of the cited portions of Aksay.

Paragraph [0055] of Aksay states:

> [0055] More specifically, in order to promote *growth of a mesostructured inorganic on these substrates*, an aqueous recipe that includes an excess of adsorbing cetyltrimethyl ammonium chloride (CTAC) surfactant and a dilute acidic solution of tetraethoxy silane (TEOS) inorganic precursor is used. Inorganic solute concentrations are purposefully kept dilute in order to decrease the rate of homogeneous nucleation to such an extent that the more thermodynamically favored heterogeneous nucleation route is dominant. The procedure involved dissolving TEOS liquid in an

> aqueous solution of CTAC and hydrochloric acid. Typical molar ratios are 1 TEOS:2 CTAC:9.2 HCl:1000 H_2O. [Emphasis added.]

Paragraph [0055] relates to "growth of a mesostructured *inorganic*," and "a mesostructured *inorganic*" is not a "biomolecule" even by the Examiner's definition of a biomolecule to mean "any organic molecule that is an essential part of a living organism."

Paragraph [0004] of Aksay states:

> [0004] Biologically produced inorganic-organic composites such as bone, teeth, diatoms, and sea shells are fabricated through highly coupled (and often concurrent) synthesis and assembly. These structures are formed through template-assisted self-assembly, in which self-assembled organic material (such as proteins, or lipids, or both) form the structural scaffolding for the deposition of inorganic material. They are hierarchically structured composites in which soft organic materials are organized on length scales of 1 to 100 nm and used as frameworks for specifically oriented and shaped inorganic crystals (that is, ceramics such as hydroxyapatite, $CaCo_3$, SiO_2, and Fe_3O_4). In some cases, structurally organized organic surfaces catalytically or epitaxially induce growth of specifically oriented inorganic thin films.

Paragraph [0004] is the background of the invention of Aksay and simply explains that biologically produced materials have "structures [that] are formed through template-assisted self-assembly, in which self-assembled organic material (such as proteins, or lipids, or both) form the structural scaffolding for the deposition of inorganic material." This background of the invention does not teach or suggest that one should substitute the object of Kley (which does "disclose wherein an object can be biomolecule" - see page 3, line 14, of the Action) with a biomolecule. In fact, Aksay teaches just the opposite; to create man-made inorganic morphological structures that mimic biologically produced products of nature, but not to substitute a non-biomolecular object such as that of Kley with a biomolecule.

Abstract, first 10 lines, of Aksay states:

> A process directed to preparing surfactant-polycrystalline *inorganic nanostructured materials* having designed microscopic patterns. The

> process includes forming a polycrystalline inorganic substrate having a flat surface and placing in contact with the flat surface of the substrate a surface having a predetermined microscopic pattern. An acidified aqueous reacting solution is then placed in contact with an edge of the surface having the predetermined microscopic pattern. The solution wicks into the microscopic pattern by capillary action. [Emphasis added.]

Abstract, first 10 lines, of Aksay relates to "[a] process directed to preparing surfactant-polycrystalline *inorganic nanostructured materials* having designed microscopic patterns" and "*inorganic nanostructured materials*" are not a "biomolecule" even by the Examiner's definition of a biomolecule to mean "any organic molecule that is an essential part of a living organism."

Furthermore, Examiner has acknowledged that Kley does not disclose "aligning a biomolecule in a parallel manner on a surface." See page 3, line 15, of the Action. The Examiner attempts to fill this gap in Kley by stating "Aksay teaches ... alignment of the biomolecule (the alignment of nanostructures which disclosed by Aksay can be biomolecule) (page 2, column 2, [0023]; page 3, column 2, [0036])." See page 2, lines 9-13, of the Action. Let us review paragraphs [0023] and [0036] of Aksay.

Paragraph [0023] of Aksay states:

> [0023] It is still another object of this invention to provide a nanolithographic process that allows the direction of growth of these *tubules* to be guided to form highly aligned, designed nanostructures. [Emphasis added.]

Paragraph [0036] of Aksay states:

> [0036] FIG. 4 shows TEM images of a mesostructured silica film grown on mica. Both images are in a transverse orientation with respect to the film and reveal hexagonal packing of *tubules aligned parallel to the substrate*. The image in (A) reveals a slight elliptical distortion of the tubules suggesting that the films are strained, that is, compressed in the direction normal to the template. [Emphasis added.]

Paragraph [0023] of Aksay states that the "[i]t is still another object of this invention to provide a nanolithographic process that allows the direction of growth of these *tubules* to be guided to form highly aligned, designed nanostructures." This paragraph refers to forming highly aligned, designed nanostructures made of "tubules" which are "*surfactant-silicate* nanotubule structures" (see claim 3), but it does *not* read on the limitation "aligning a biomolecule in a parallel manner on a surface by molecular combing" as a "surfactant-silicate" tubules are not a "biomolecule" even by the Examiner's definition of a biomolecule to mean "any organic molecule that is an essential part of a living organism."

In short, the Examiner has acknowledged that Kley does not disclose "aligning a biomolecule in a parallel manner on a surface," and Aksay discloses alignment of surfactant-silicate nanotubules, but not "aligning a *biomolecule* in a parallel manner on a *surface by molecular combing*" recited in claim 1. Please note that *both* Kley and Aksay fail to disclose alignment "by molecular combing." Thus, Applicants respectfully submit that neither Kley nor Aksay disclose the limitation "aligning a biomolecule in a parallel manner on a surface by molecular combing" of claim 1 or the limitation "wherein the molecular structures are biomolecules and the molecular combining comprises attachment of the biomolecules to a surface and alignment of the biomolecules" of claim 24.

Claims 8-11 were rejected as being obvious over Kley in view of Aksay, as applied to claim 1, further in view of Grand. This rejection is respectfully traversed.

Claims 8-11 depend directly or indirectly from claim 1. Grand does not fill the gaps in Kley and Aksay. Thus, claims 8-11 should also be allowable as claims 1-2, 4-7, 12-13, 24-26 and 28-29 should now be allowable.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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Exhibit 1

Department of Chemical Engineering

People: Faculty

Ilhan A. Aksay

Professor

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Honors and Awards

- National (Turkish) Medal of Science, Tubitak, Turkey, 2001
- Edward C. Henry Award, the American Ceramic Society, 2000
- Charles M.A. Stine Award, American Institute of Chemical Engineers, 1997
- Richard M. Fulrath Award, American Ceramic Society, 1987

Concurrent University Appointments

- Associated Faculty, Department of Civil and Environmental Engineering
- Associated Faculty, Department of Mechanical and Aerospace Engineering
- Associated Faculty, Princeton Environmental Institute

Publications

Research Interests

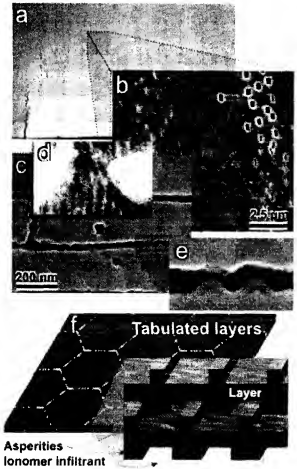
Materials processing with complex fluids is the central theme of our research activities. Complex fluids such as colloids and/or amphiphilic solutions spontaneously self-assemble to produce ordered nanostructures, an essential step in the design and processing of materials [D.M. Dabbs, I.A. Aksay, *Annu. Rev. Phys. Chem.* **51** 601 (2000)]. Many of our activities draw inspiration from biological systems (see following figure) [R.Z. Wang, Z. Suo, A.G.

Evans, N. Yao, I.A. Aksay, *J. Mater. Res.* **16** 2485 (2001)]. Like the biological analogs that provide inspiration, our goal is to shape new systems that are multifunctional, "smart" in their ability to detect and respond to changes in environmental conditions, and capable of self-healing.

Guided self-assembly of nanostructured composites. Although self-assembly provides locally ordered nanostructures similar to those observed in biological systems, global order is not attained due to the statistical nature of the ordering process. We explore the role of electrohydrodynamic effects to guide the global order by a variety of techniques that have derived their fundamental understanding from joint studies with D.A. Saville [W.D. Ristenpart, I.A. Aksay, D.A. Saville, *Phys. Rev. Lett.* **90** 128303 (2003)]. Colloidal patterning through cone-jet printing is one technique that offers the potential to produce patterns at the nanometer scale rapidly and over large areas.

Self-healing materials. Man-made materials lack the ability for self-repair; whereas biologically produced materials sense and repair defects through cellular activities. Concepts generated from model studies provide new approaches for the development of man-made materials with self-repair functions. Our synthetic analogs are built with arrays of microreactors through pixelated structures similar to those used in LCD technology. For instance, when an organic/inorganic hybrid coating is damaged, the damaged region heals spontaneously [N. Yao, A.Y. Ku, H. Nakagawa, T. Lee, D.A. Saville, I.A. Aksay, *Chem. Mater.* **12** 1536 (2000)]. Further, the rate of self-repair is enhanced with the application of weak electrical fields ($\sim 10^2$ V/m). In a second example, we partially mimic the process of blood clotting as a process of colloidal aggregation at a defect site. We then make this a permanent protective layer, for instance, through the electrodeposition of a metal binder in the interstitials of the colloidal aggregate. In both approaches the mechanisms are not yet fully understood.

Microsensors and actuators. Our goal is to develop arrays of piezoelectric microcantilevers (e.g., PbO-ZrO_2-TiO_2 (PZT)) that replicate the process of gathering physical and chemical metrics *in vivo*. We explore the feasibility of using arrays of nanocomposite microcantilevers [C.R. Martin, I.A. Aksay, *J. Phys. Chem. B* **107** 4261 (2003)] as biosensors that are capable of simultaneously measuring, in real time, multiple biophysical and biochemical properties of fluids in the human body [W.Y. Shih, X. Li, H. Gu, W.-H. Shih, I.A. Aksay, *J. Appl. Phys.* **89** 1497 (2001)]. A nanostructured coating (L_3 templated silica) gives enhanced sensitivity due to the presence of features from 5 to 30 nm in size that, in turn, give rise to a large effective surface-area (>1000 m^2/g).



(a, b, c) Tabular and layered structure of nacre from abalone shown at three magnifications. (d, e) Distributed deformation, displayed by the opening of gaps between all tablets by a fixed strain, is regulated through nanoscaled pillars (d) and asperities (e). (f) A synthetic model.

length scales of 1-100 nm function as frameworks for the growth of specifically oriented and shaped inorganics (e.g., $CaCO_3$, SiO_2, Fe_3O_4, hydroxyapatite) with small unit cells. The high modulus inorganic phase provides the stiffness while the organic phase enhances toughness. Although the principle of hierarchical design has been applied to synthetic composites, the smallest length scale readily accessible is on the micron scale.

The Ceramics Materials Laboratory is interested in refining existing techniques and developing new ones which allow structural control at a variety of length scales from nanometer to macroscopic. Active research areas include **Self-Assembly and Patterning**, **Self-Healing Materials**, and **Biosensors**.

II. Self-assembly and Templating Processes

Biological systems are known to self-assemble into organized structures at many length scales. At the smallest levels, the resulting structures sometimes act as templates for the growth of other materials. The end result is a layered composite with several levels of structural organization. For example, the structure of an abalone shell consists of layered plates of $CaCO_3$ (~200 nm) held together by a much thinner (<10 nm) "mortar" of organic template. Our interest in the structural properties of seashell is described in the project *Mechanical Properties of Seashell*.

Another class of biogenic materials in which self-assembly and templating lead to a macroscopic materials system of specialized application is bone. In the project **Bone Implant Technology**, we seek to use the techniques of rapid prototyping to tailor bone implants with composition and structure similar to those of natural bone.

III. Structure-property relationship modeling

A host of structure-property models exist to describe the mechanical, electromagnetic, optical and other properties of material systems. However, the biologically-inspired introduction of structural order at multiple length scales presents a problem. Since many material properties (e.g., fracture) do not scale linearly with size, structure at the nanometer scale leads to properties fundamentally different from those based on simple mixing rules or extrapolation from the bulk properties of the constituents.